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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,223	11/27/2001	Jennifer L. Hillman	PF-0425-1 DIV	4146

22428 7590 12/13/2004

FOLEY AND LARDNER  
SUITE 500  
3000 K STREET NW  
WASHINGTON, DC 20007

EXAMINER
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UNGAR, SUSAN NMN

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 12/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	09/996,223		HILLMAN ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	Susan Ungar		1642	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 10 September 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☐ Claim(s) 1,2,11,17,18,20,23,26,27,30-32 and 34-45 is/are pending in the application.
- 4a) Of the above claim(s) 11,18,20,23,26,27,30-32 and 34-45 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1,2,17 and 18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

1. The Amendment filed September 10, 2004 in response to the Office Action of May 10, 2004 is acknowledged and has been entered. Claim 1 has been amended. Claims 1, 2, 17, 18 are currently under prosecution.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. The following rejections are maintained:

***Claim Rejections –35 USC 112***

4. Claims 1, 2, 17 and 18 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the Paper mailed May 10, 2004, Section 5, pages 4-8.

Applicant argues that definitive structural features have been disclosed in the specification, specifically potential casein kinase II phosphorylation sites of the protein represented by SEQ ID NO:1, potential protein kinase C phosphorylation sites and potential tyrosine kinase phosphorylation sites as well as potential citrate synthase signature sites and points to page 14, lines 15-19. The argument has been considered but has not been found persuasive because Applicant is arguing limitations not recited in the claims as currently constituted. Further, the argument has been considered but has not been found persuasive because “potential” sites are not definitive sites. Further, although Applicant points to potential sites, the specification does not teach conserved regions which are critical to the structure and function of the genus, there is no disclosure of sites at which variability may be tolerated, there is no information regarding the relation of structure to function. The argument has been considered but has not been found persuasive and the rejection is maintained.

***New and Maintained Grounds of Rejection***

***Claim Rejections –35 USC 112***

5. Claims 1, 2, 17, 18 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the Paper mailed May 10, 2004, Section 6, pages 8-11 and further for the reasons below.

Applicant argues that amendment of claim 1 to delete claims to biologically active fragments, immunogenic fragments and to change the recitation of the claim from 90% identity to “an” amino acid sequence of SEQ ID NO:1 to 95% identity to the full length amino acid sequence of SEQ ID NO:1 obviates the instant rejection. Applicant again points to page 14, lines 15-19 to support definite structural features and conserved regions.

The argument has been considered but has not been found persuasive as drawn to definite structural features and conserved regions for the reasons set forth above. The applicant does not teach how to make and use the claimed invention for the reasons previously set forth.

Further, the claims as currently constituted, that is naturally occurring polypeptides comprising an amino acid sequence at least 95% identical to the full length amino acid sequence depicted in SEQ ID NO:1 reads on splice variants of SEQ ID NO:1. The unpredictability of function of splice variants is well known in the art. For example, Hirashima (Int. Arch. Allergy Immunol., 2000, Suppl 1:6-9) discloses that there are multiple isoforms of ecalectin/galectin-9 (page 8, first column second paragraph, lines 10-16), and “it cannot be excluded that each isoform exhibits different biological activity” (page 8, second column, lines 6-7). Benedict et al (J. Exp. Medicine, 2001, 193(1)89-99) specifically teach that two splice isoforms of terminal deoxynucleotidy transferase (a long form and a short

form) enter the nucleus but have different activity, the long form does not catalyze nontemplated nucleotide addition but rather modulates the activity of the short form (see abstract). Jiang et al (JBC, 2003, 278(7) 4763-4769 specifically teach that the type 3  $\text{Ca}^{2+}$  release channel, RyR3 exhibits strikingly different pharmacologic and functional properties depending on the tissues in which it resides. Upon examination, seven tissue specific alternatively spliced variants of RyR3 were detected. One of the variants was unable to form a functional channel but was able to suppress the activity of a different release channel. The authors conclude that tissue-specific expression of RyR3 splice variants is likely to account for some of the pharmacologic and functional heterogeneities of RyR3 (see abstract). These references serve to demonstrate that one of skill in the art cannot predict the biological activity of splice variants based on the biological activity of the wild-type protein or a single protein isoform.

Further, even if the claimed invention was not a naturally occurring splice variant of SEQ ID NO:1, absent objective, a percentage sequence similarity of less than 100 % is not deemed to reasonably support, to one skilled in the art, whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function and therefore lacks support regarding utility and/or enablement. Several

publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Iyer et al. Genome Biology 2001 2 (12) pages 1-11; and Baker et al. Science, October, 2001, Vol. 294 pages 93-95. However, this level of objective evidence is absent here.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which allow one of skill in the art to predict how to use the claimed invention with reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed inventions with a reasonable expectation of success.

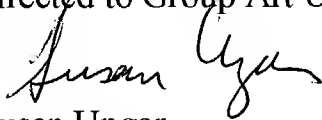
5. All other rejections and objections recited in the previous paper are hereby withdrawn.
6. No claims allowed.
7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (703) 872-9306.

Art Unit: 1642

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 872-9306.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

A handwritten signature in black ink, appearing to read "Susan Ungar". The signature is fluid and cursive, with the first name "Susan" and last name "Ungar" clearly distinguishable.

Susan Ungar  
Primary Patent Examiner  
November 4, 2004